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MORRISON & FOERSTER LLP				EXAMINER		
425 MARKET STREET SAN FRANCISCO, CA 94105-2482				EINSMANN, JUL	IET CAROLINE	
				ART UNIT	PAPER NUMBER	
				1634		
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Please find below and/or attached an Office communication concerning this application or proceeding.

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1		Application No.	Applicant(s)	
		09/538,864	CHO ET AL.	
C	ffice Action Summary	Examiner	Art Unit	
		Juliet C Einsmann	1634	
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	Certified copies of the priority documents	s have been received.		
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15)[_] ACKNO Attachment(s)	wledgment is made of a claim for domesti	c priority under 35 U.S.C.	§§ 120 and/or 121.	
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2) 🔲 Notice of Dr	afterences Cited (P10-892) aftsperson's Patent Drawing Review (PT0-948) Disclosure Statement(s) (PT0-1449) Paper No(s) <u>17</u>	5) Notice of	Summary (PTO-413) Paper No Informal Patent Application (PT	

Continuation Sheet (PTO-326)

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Continuation of Disposition of Claims: Claims pending in the application are 32-34,36-43,77,79-86,112-116,118-120,122,124,126,128,130,132-136,138-140,142,144,146,148 and 150-157.

Claims rejected are 32-34,36-43,77,79-86,112-116,118-120,122,124,126,128,130,132-136,138-140,142,144,146,148 and 150-157.

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DETAILED ACTION

1. This action is written in response applicant's correspondence submitted 5/23/02, paper numbers 20. Claims 32, 36, 37, 38, 43, 77, 79, 80, 81, 82, 115, 119, 130, 133, 135, and 149 have been amended, claims 35, 78, 117, 121, 123, 125, 127, 129, 131, 137, 141, 143, 145, 147, and 149 have been canceled, and claims 150-157 have been added. Claims 32-34, 36-43, 77, 79-86, 112-116, 118-120, 122, 124, 126, 128, 130, 132-136, 138-140, 142, 144, 146, 148, and 150-157 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

- 2. The following is a quotation of the first paragraph of 35 U.S.C. 112:
 - The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
- 3. Claims 32-34, 36-38, 41-43, 77, 79-81, 84-86, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, and 148 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are drawn to monocot transgenic plants and seeds which comprise a promoter active in said plant operably linked to a nucleic acid encoding a thioredoxin polypeptide selected from the group consisting of barley, rice, Arabidopsis, soybean, wheat,

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tobacco, and Brassica thioredoxins. In order to be in possession of such plants, at the very least applicants must be in possession of nucleic acids encoding the appropriate thioredoxin polypeptides from the appropriate plant species. The prior art provides only nucleic acids encoding thioredoxin h molecules from each of the recited groups of plants, yet the instant claims encompass transgenic plants comprising a nucleic acid encoding any type of thioredoxin, including thioredoxin type m or thioredoxin type f. The instant specification, in example 6 provide a nucleic acid which encodes a single barley thioredoxin h (SEQ ID NO: 24).

Thus, of all of the possible nucleic acids encoding all of the different types thioredoxins in monocot plants, applicant is in express possession of only nucleic acids encoding thioredoxin h polypeptides from the recited plant types. Neither Applicant nor the prior art provide the cDNA molecules encoding any other types of thioredoxin molecules from the recited species. Neither Applicant nor the prior art provide any nucleic acid encoding thioredoxin polypeptides from the recited species that encode other types thioredoxin molecules besides thioredoxin h polypeptides.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

"...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

"...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

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In the application at the time of filing, there is no record or description which would demonstrate conception or written description of transgenic plants comprising any and all possible nucleic acids encoding thioredoxin molecules which has nucleic acids modified by addition, insertion, deletion, substitution or inversion with the molecules disclosed in the cited prior art or herein in example 6 but retaining correlative function in the claimed products.

- 4. The following is a quotation of the second paragraph of 35 U.S.C. 112:
 The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
- 5. Claims 152-153 and 156-157 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite over the recitation "The transgenic plant of claim 77" because claim 77 does not recite a transgenic plant, it recites transgenic seeds or grains. It is thus unclear if applicant is intending to claim transgenic plants or seeds.

Claim Rejections - 35 USC § 103

- 6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
- 7. Claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 113, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 133, 134, 136, 138, 140, 142, 144, 146, and 148 are rejected under 35 U.S.C. 103(a) as being unpatentable over van Ooijen et al. (US 5543576) in view of

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Ishiwatari et al. (Planta, 1995, 195(3)456-463), and optionally, both of these further in view of Shi et al. (Plant Molecular Biology, 1996, 32:653-662).

Van Ooijen et al. teach transgenic plants which express genes of interest (ABSTRACT). In particular, Van Ooijen et al. teach monocot transgenic plants, specifically reciting a variety of plant types, including maize, barley, wheat, oats, rice, and grasses (Col. 6, lines 10-18). Van Ooijen et al. teach that the plants are useful for the production of any polypeptide of interest, including enzymes and industrial proteins (Col. 4, line 65-Col. 5, line 34). Van Ooijen et al. teach specifically teaches the production of seeds from said monocot plants, further teaching the use of seed specific promoters, especially from storage genes (Col. 7, lines 58-60) and that the protein of interest should expressed in a way that allows optimal stability of the protein during seed maturation, and teach targeting to intracellular compartments (Col. 8, lines 7-10).

Van Ooijen et al. do not teach transgenic plants expressing thioredoxins.

Ishiwatari *et al.* teach the cDNA encoding a thioredoxin h polypeptide from the monocot rice (Fig. 3). Further, Ishiwatari *et al.* teach methods in which the polypeptide was over expressed in E. coli (p. 457).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced transgenic plants producing a monocot thioredoxin such as the one taught by Ishiwatari *et al.* using any of the routine methods taught by Van Ooijen et al. The ordinary practitioner would have been motivated by the successful expression of thioredoxins in E. coli by Ishiwatari *et al.*, by a desire to produce industrially useful thioredoxin polypeptide, and by the teachings the use transgenic plants for the production of industrial enzymes as taught by Van Ooijen et al. Thioredoxins were widely known at the time the

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invention was made to be enzymes with many industrial uses, including in the flour making industry, as is admitted by the instant specification, and Van Ooijen et al. specifically teaches the advantages of such a method for the production of polypeptides stating "the present invention allows for the reduction of costs associated with the production, storage and use of a variety of enzymes (Col. 3, lines 65-67)." In the absence of a secondary consideration, such as an unexpected result, the instantly broadly claimed invention is free of the prior art. With regard to the claims specifically drawn to rye, millet, triticale and sorghum transgenic plants, at the time the invention was made, the selection of one of any number of plant species to be transformed for the expression of industrial enzymes would have been routine, a matter solely of experimental design. The ordinary practitioner would have recognized that the teachings of van Ooijen et al. encompass the production of transgenic plants in any number of monocots and edible grains as discussed above. Rye, millet, triticale and sorghum are such a plants, and thus the transformation of these plants is considered to be encompassed by the teachings of van Ooijin et al.

While the examiner believes that adequate motivate to make the claimed invention is provided by the above rejection, Shi *et al.* provide further motivation to make transgenic plants that produce thioredoxin h. Shi *et al.* experiments in which they transformed tobacco plants with thioredoxin h for the purpose of studying thioredoxin h activity in plants (p. 654 and 657). Shi *et al.* further teach that thioredoxins are active in many biochemical processes in plants (p. 654). Shi *et al.* teach eight day old plants and mature plants with pods, and further teach analysis of transgenic seeds (p. 658, Col. 2). Thus, the combined teachings of van Ooijen et al., Ishiwatari *et al.* and Shi *et al.* would have further motivated the production of monocot plants expressing

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transgenic monocot thioredoxin h molecules. The teachings of Ishiwatari *et al.* provide a monocot thioredoxin of interest, the teachings of van Ooijen specifically provide methodology for the transformation of monocots, and Shi *et al.* demonstrate that the production of transgenic plants producing thioredoxin h is of interest in elucidating the functionality of thioredoxin h in plants. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made transgenic plants expressing these thioredoxin h molecules. The ordinary practitioner would have been motivated to transform transgenic plants with these molecules in order to further study the biological function of the thioredoxin h polypeptides plants, or as an alternative method for producing thioredoxin h polypeptides for study. The ordinary practitioner would have been motivated by the success of Shi *et al.*'s expression of thioredoxin to extend this method to the thioredoxin molecules taught by Ishiwatari *et al.* The ordinary practitioner would have also been motivated by the teachings of van Ooijen et al. to produce specifically monocot plants producing thioredoxin h in order to study the activity of this polypeptide in monocot plants.

Thus for all of these reasons, the rejected claims are prima facie obvious in view of the prior art.

8. Claims 32, 33, 34, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 119, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 139, 140, 142, 144, 146, and 148 rejected under 35 U.S.C. 103(a) as being unpatentable over van Ooijen et al. (US 5543576) in view of Gautier *et al.* (1998, European Journal of Biochemistry, 252:314-324), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662).

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Van Ooijen et al. teach transgenic plants which express genes of interest (ABSTRACT). In particular, Van Ooijen et al. teach monocot transgenic plants, specifically reciting a variety of plant types, including maize, barley, wheat, oats, rice, and grasses (Col. 6, lines 10-18). Van Ooijen et al. teach that the plants are useful for the production of any polypeptide of interest, including enzymes and industrial proteins (Col. 4, line 65-Col. 5, line 34). Van Ooijen et al. teach specifically teaches the production of seeds from said monocot plants, further teaching the use of seed specific promoters, especially from storage genes (Col. 7, lines 58-60) and that the protein of interest should expressed in a way that allows optimal stability of the protein during seed maturation, and teach targeting to intracellular compartments (Col. 8, lines 7-10).

Van Ooijen et al. do not teach transgenic plants expressing thioredoxins.

Gautier *et al.* teach the cDNA encoding a thioredoxin h polypeptide from the monocot wheat (Fig. 1). Further, Gautier *et al.* teach methods in which the polypeptide was over expressed in E. coli (p. 317-318).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced transgenic plants producing a monocot thioredoxin such as the one taught by Gautier *et al.* using any of the routine methods taught by van Ooijen et al. The ordinary practitioner would have been motivated by the successful expression of thioredoxins in E. coli by Gautier *et al.*, by a desire to produce industrially useful thioredoxin polypeptide, and by the teachings the use transgenic plants for the production of industrial enzymes as taught by van Ooijen. Thioredoxins were widely known at the time the invention was made to be enzymes with many industrial uses, including in the flour making industry, as is admitted by the instant specification, and Van Ooijen et al. specifically teaches the advantages of such a method for the

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production of polypeptides stating "the present invention allows for the reduction of costs associated with the production, storage and use of a variety of enzymes (Col. 3, lines 65-67)." In the absence of a secondary consideration, such as an unexpected result, the instantly broadly claimed invention is free of the prior art. With regard to the claims specifically drawn to rye, millet, triticale and sorghum transgenic plants, at the time the invention was made, the selection of one of any number of plant species to be transformed for the expression of industrial enzymes would have been routine, a matter solely of experimental design. The ordinary practitioner would have recognized that the teachings of van Ooijen et al. encompass the production of transgenic plants in any number of monocots and edible grains as discussed above. Rye, millet, triticale and sorghum are such a plants, and thus the transformation of these plants is considered to be encompassed by the teachings of van Ooijin et al.

While the examiner believes that adequate motivate to make the claimed invention is provided by the above rejection, Shi *et al.* provide further motivation to make transgenic plants that produce thioredoxin h. Shi *et al.* experiments in which they transformed tobacco plants with thioredoxin h for the purpose of studying thioredoxin h activity in plants (p. 654 and 657). Shi *et al.* further teach that thioredoxins are active in many biochemical processes in plants (p. 654). Shi *et al.* teach eight day old plants and mature plants with pods, and further teach analysis of transgenic seeds (p. 658, Col. 2). Thus, the combined teachings of van Ooijen et al., Gautier *et al.* and Shi *et al.* would have further motivated the production of monocot plants expressing transgenic monocot thioredoxin h molecules. The teachings of Gautier *et al.* provide a monocot thioredoxin of interest, the teachings of Van Ooijen provide methodology for the transformation of monocots, and Shi *et al.* demonstrate that the production of transgenic plants producing

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thioredoxin h is of interest in elucidating the functionality of thioredoxin h in plants. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made transgenic plants expressing these thioredoxin h molecules. The ordinary practitioner would have been motivated to transform transgenic plants with these molecules in order to further study the biological function of the thioredoxin h polypeptides plants, or as an alternative method for producing thioredoxin h polypeptides for study. The ordinary practitioner would have been motivated by the success of Shi *et al.*'s expression of thioredoxin to extend this method to the thioredoxin molecules taught by Gautier *et al.* The ordinary practitioner would have also been motivated by the teachings of Van Ooijen et al. to produce specifically monocot plants producing thioredoxin h in order to study the activity of this polypeptide in monocot plants.

Thus for all of these reasons, the rejected claims are prima facie obvious in view of the prior art.

9. Claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, and 152 are rejected under 35 U.S.C. 103(a) as being unpatentable over van Ooijen et al. (US 5543576) in view of Rivera-Madrid et al. (PNAS USA, 92:5620-5624 (1995)), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662).

Van Ooijen et al. teach transgenic plants which express genes of interest (ABSTRACT). In particular, Van Ooijen et al. teach monocot transgenic plants, specifically reciting a variety of plant types, including maize, barley, wheat, oats, rice, and grasses (Col. 6, lines 10-18). Van Ooijen et al. teach that the plants are useful for the production of any polypeptide of interest,

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including enzymes and industrial proteins (Col. 4, line 65-Col. 5, line 34). Van Ooijen et al. teach specifically teaches the production of seeds from said monocot plants, further teaching the use of seed specific promoters, especially from storage genes (Col. 7, lines 58-60) and that the protein of interest should expressed in a way that allows optimal stability of the protein during seed maturation, and teach targeting to intracellular compartments (Col. 8, lines 7-10).

Van Ooijen et al. do not teach transgenic plants expressing thioredoxins.

Rivera-Madrid *et al.* teach five cDNAs encoding a thioredoxin h polypeptide from the Arabidopsis thaliana (p. 5620). Further, Rivera-Madrid *et al.* teach methods in which the polypeptide was over expressed in E. coli (p. 5621).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced transgenic plants producing a thioredoxin such as the one taught by Rivera-Madrid *et al.* using any of the routine methods taught by Van Ooijen et al. The ordinary practitioner would have been motivated by the successful expression of thioredoxins in E. coli by Rivera-Madrid *et al.*, by a desire to produce industrially useful thioredoxin polypeptide, and by the teachings the use transgenic plants for the production of industrial enzymes as taught by Van Ooijen et al. Thioredoxins were widely known at the time the invention was made to be enzymes with many industrial uses, including in the flour making industry, as is admitted by the instant specification, and Van Ooijen et al. specifically teaches the advantages of such a method for the production of polypeptides stating "the present invention allows for the reduction of costs associated with the production, storage and use of a variety of enzymes (Col. 3, lines 65-67)." In the absence of a secondary consideration, such as an unexpected result, the instantly broadly claimed invention is free of the prior art. With regard to the claims specifically drawn to rye,

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millet, triticale and sorghum transgenic plants, at the time the invention was made, the selection of one of any number of plant species to be transformed for the expression of industrial enzymes would have been routine, a matter solely of experimental design. The ordinary practitioner would have recognized that the teachings of van Ooijen et al. encompass the production of transgenic plants in any number of monocots and edible grains as discussed above. Rye, millet, triticale and sorghum are such a plants, and thus the transformation of these plants is considered to be encompassed by the teachings of van Ooijin et al.

While the examiner believes that adequate motivate to make the claimed invention is provided by the above rejection, Shi *et al.* provide further motivation to make transgenic plants that produce thioredoxin h. Shi *et al.* experiments in which they transformed tobacco plants with thioredoxin h for the purpose of studying thioredoxin h activity in plants (p. 654 and 657). Shi *et al.* further teach that thioredoxins are active in many biochemical processes in plants (p. 654). Shi *et al.* teach eight day old plants and mature plants with pods, and further teach analysis of transgenic seeds (p. 658, Col. 2). Thus, the combined teachings of van Ooijen et al., Rivera-Madrid *et al.* and Shi *et al.* would have further motivated the production of monocot plants expressing transgenic thioredoxin h molecules. The teachings of Rivera-Madrid *et al.* provide a thioredoxin of interest, the teachings of van Ooijen specifically provide methodology for the transformation of monocots, and Shi *et al.* demonstrate that the production of transgenic plants producing thioredoxin h is of interest in elucidating the functionality of thioredoxin h in plants. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made transgenic plants expressing these thioredoxin h molecules. The ordinary practitioner would have been motivated to transform transgenic plants with these

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molecules in order to further study the biological function of the thioredoxin h polypeptides plants, or as an alternative method for producing thioredoxin h polypeptides for study. The ordinary practitioner would have been motivated by the success of Shi *et al.*'s expression of thioredoxin to extend this method to the thioredoxin molecules taught by Rivera-Madrid *et al.*The ordinary practitioner would have also been motivated by the teachings of van Ooijen et al. to produce specifically monocot plants producing thioredoxin h in order to study the activity of this polypeptide in monocot plants.

Thus for all of these reasons, the rejected claims are prima facie obvious in view of the prior art.

10. Claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 151, and 153 are rejected under 35 U.S.C. 103(a) as being unpatentable over van Ooijen et al. (US 5543576) in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662).

Van Ooijen et al. teach transgenic plants which express genes of interest (ABSTRACT). In particular, Van Ooijen et al. teach monocot transgenic plants, specifically reciting a variety of plant types, including maize, barley, wheat, oats, rice, and grasses (Col. 6, lines 10-18). Van Ooijen et al. teach that the plants are useful for the production of any polypeptide of interest, including enzymes and industrial proteins (Col. 4, line 65-Col. 5, line 34). Van Ooijen et al. teach specifically teaches the production of seeds from said monocot plants, further teaching the use of seed specific promoters, especially from storage genes (Col. 7, lines 58-60) and that the protein of interest should expressed in a way that allows optimal stability of the protein during seed maturation, and teach targeting to intracellular compartments (Col. 8, lines 7-10).

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Van Ooijen et al. do not teach transgenic plants expressing thioredoxins.

Shi et al. teach nucleic acids encoding thioredoxin h polypeptides from soybean (p. 564). Shi et al. further teach experiments in which they transformed tobacco plants with thioredoxin h for the purpose of studying thioredoxin h activity in plants (p. 654 and 657). Shi et al. further teach that thioredoxins are active in many biochemical processes in plants (p. 654). Shi et al. teach eight day old plants and mature plants with pods, and further teach analysis of transgenic seeds (p. 658, Col. 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced monocot transgenic plants producing a thioredoxin such as the one taught by Shi *et al.* using any of the routine methods taught by Van Ooijen et al. The ordinary practitioner would have been motivated by the successful expression of thioredoxins in tobacco plants by Shi *et al.*, by a desire to produce industrially useful thioredoxin polypeptide, and by the teachings the use transgenic plants for the production of industrial enzymes as taught by Van Ooijen et al. Thioredoxins were widely known at the time the invention was made to be enzymes with many industrial uses, including in the flour making industry, as is admitted by the instant specification, and Van Ooijen et al. specifically teaches the advantages of such a method for the production of polypeptides stating "the present invention allows for the reduction of costs associated with the production, storage and use of a variety of enzymes (Col. 3, lines 65-67)." In the absence of a secondary consideration, such as an unexpected result, the instantly broadly claimed invention is free of the prior art.

Furthermore, since Shi et al. demonstrate that the production of transgenic plants producing thioredoxin h is of interest in elucidating the functionality of thioredoxin h in plants, it

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would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made additional transgenic monocot plants expressing these thioredoxin h molecules. The ordinary practitioner would have been motivated to transform transgenic plants with these molecules in order to further study the biological function of the thioredoxin h polypeptides plants, or as an alternative method for producing thioredoxin h polypeptides for study. The ordinary practitioner would have been motivated by the success of Shi *et al.*'s expression of thioredoxin to extend this method other plant species. The ordinary practitioner would have also been motivated by the teachings of van Ooijen et al. to produce specifically monocot plants producing thioredoxin h in order to study the activity of this polypeptide in monocot plants.

With regard to the claims specifically drawn to rye, millet, triticale and sorghum transgenic plants, at the time the invention was made, the selection of one of any number of plant species to be transformed for the expression of industrial enzymes would have been routine, a matter solely of experimental design. The ordinary practitioner would have recognized that the teachings of van Ooijen et al. encompass the production of transgenic plants in any number of monocots and edible grains as discussed above. Rye, millet, triticale and sorghum are such a plants, and thus the transformation of these plants is considered to be encompassed by the teachings of van Ooijin et al. Thus, the combined teachings of van Ooijen et al. and Shi *et al.* would have further motivated the production of monocot plants expressing transgenic thioredoxin h molecules.

Thus for all of these reasons, the rejected claims are prima facie obvious in view of the prior art.

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11. Claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 154, and 156 are rejected under 35 U.S.C. 103(a) as being unpatentable over van Ooijen et al. (US 5543576) in view of Brugidou et al. (Mol. Gen. Genet (1993) 238:285-293), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662).

Van Ooijen et al. teach transgenic plants which express genes of interest (ABSTRACT). In particular, Van Ooijen et al. teach monocot transgenic plants, specifically reciting a variety of plant types, including maize, barley, wheat, oats, rice, and grasses (Col. 6, lines 10-18). Van Ooijen et al. teach that the plants are useful for the production of any polypeptide of interest, including enzymes and industrial proteins (Col. 4, line 65-Col. 5, line 34). Van Ooijen et al. teach specifically teaches the production of seeds from said monocot plants, further teaching the use of seed specific promoters, especially from storage genes (Col. 7, lines 58-60) and that the protein of interest should expressed in a way that allows optimal stability of the protein during seed maturation, and teach targeting to intracellular compartments (Col. 8, lines 7-10).

Van Ooijen et al. do not teach transgenic plants expressing thioredoxins.

Brugidou et al. teach a cDNAs encoding a thioredoxin h polypeptide from the tobacco (p. 287 and Fig. 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced transgenic plants producing a thioredoxin such as the one taught by Brugidou *et al.* using any of the routine methods taught by Van Ooijen et al. The ordinary practitioner would have been motivated by a desire to produce industrially useful thioredoxin polypeptide, and by the teachings the use transgenic plants for the production of

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industrial enzymes as taught by Van Ooijen et al. Thioredoxins were widely known at the time the invention was made to be enzymes with many industrial uses, including in the flour making industry, as is admitted by the instant specification, and Van Ooijen et al. specifically teaches the advantages of such a method for the production of polypeptides stating "the present invention allows for the reduction of costs associated with the production, storage and use of a variety of enzymes (Col. 3, lines 65-67)." In the absence of a secondary consideration, such as an unexpected result, the instantly broadly claimed invention is free of the prior art. With regard to the claims specifically drawn to rye, millet, triticale and sorghum transgenic plants, at the time the invention was made, the selection of one of any number of plant species to be transformed for the expression of industrial enzymes would have been routine, a matter solely of experimental design. The ordinary practitioner would have recognized that the teachings of van Ooijen et al. encompass the production of transgenic plants in any number of monocots and edible grains as discussed above. Rye, millet, triticale and sorghum are such a plants, and thus the transformation of these plants is considered to be encompassed by the teachings of van Ooijin et al.

While the examiner believes that adequate motivate to make the claimed invention is provided by the above rejection, Shi *et al.* provide further motivation to make transgenic plants that produce thioredoxin h. Shi *et al.* experiments in which they transformed tobacco plants with thioredoxin h for the purpose of studying thioredoxin h activity in plants (p. 654 and 657). Shi *et al.* further teach that thioredoxins are active in many biochemical processes in plants (p. 654). Shi *et al.* teach eight day old plants and mature plants with pods, and further teach analysis of transgenic seeds (p. 658, Col. 2). Thus, the combined teachings of van Ooijen et al., Brugidou *et*

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al. and Shi et al. would have further motivated the production of monocot plants expressing transgenic thioredoxin h molecules. The teachings of Brugidou et al. provide a thioredoxin of interest, the teachings of van Ooijen specifically provide methodology for the transformation of monocots, and Shi et al. demonstrate that the production of transgenic plants producing thioredoxin h is of interest in elucidating the functionality of thioredoxin h in plants. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made transgenic plants expressing these thioredoxin h molecules. The ordinary practitioner would have been motivated to transform transgenic plants with these molecules in order to further study the biological function of the thioredoxin h polypeptides plants, or as an alternative method for producing thioredoxin h polypeptides for study. The ordinary practitioner would have been motivated by the success of Shi et al.'s expression of thioredoxin to extend this method to the thioredoxin molecules taught by Brugidou et al. The ordinary practitioner would have also been motivated by the teachings of van Ooijen et al. to produce specifically monocot plants producing thioredoxin h in order to study the activity of this polypeptide in monocot plants.

Thus for all of these reasons, the rejected claims are prima facie obvious in view of the prior art.

12. Claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 155 and 157 are rejected under 35 U.S.C. 103(a) as being unpatentable over van Ooijen et al. (US 5543576) in view of Bower et al. (The Plant Cell, Vol. 8:1641-1650), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662).

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Van Ooijen et al. teach transgenic plants which express genes of interest (ABSTRACT). In particular, Van Ooijen et al. teach monocot transgenic plants, specifically reciting a variety of plant types, including maize, barley, wheat, oats, rice, and grasses (Col. 6, lines 10-18). Van Ooijen et al. teach that the plants are useful for the production of any polypeptide of interest, including enzymes and industrial proteins (Col. 4, line 65-Col. 5, line 34). Van Ooijen et al. teach specifically teaches the production of seeds from said monocot plants, further teaching the use of seed specific promoters, especially from storage genes (Col. 7, lines 58-60) and that the protein of interest should expressed in a way that allows optimal stability of the protein during seed maturation, and teach targeting to intracellular compartments (Col. 8, lines 7-10).

Van Ooijen et al. do not teach transgenic plants expressing thioredoxins.

Bower *et al.* teach two cDNA encoding a thioredoxin h polypeptide from the Brassica (p. 1462 and 1467).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced transgenic plants producing a thioredoxin such as the one taught by Bower *et al.* using any of the routine methods taught by Van Ooijen et al. The ordinary practitioner would have been motivated by a desire to produce industrially useful thioredoxin polypeptide, and by the teachings the use transgenic plants for the production of industrial enzymes as taught by Van Ooijen et al. Thioredoxins were widely known at the time the invention was made to be enzymes with many industrial uses, including in the flour making industry, as is admitted by the instant specification, and Van Ooijen et al. specifically teaches the advantages of such a method for the production of polypeptides stating "the present invention allows for the reduction of costs associated with the production, storage and use of a variety of

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enzymes (Col. 3, lines 65-67)." In the absence of a secondary consideration, such as an unexpected result, the instantly broadly claimed invention is free of the prior art. With regard to the claims specifically drawn to rye, millet, triticale and sorghum transgenic plants, at the time the invention was made, the selection of one of any number of plant species to be transformed for the expression of industrial enzymes would have been routine, a matter solely of experimental design. The ordinary practitioner would have recognized that the teachings of van Ooijen et al. encompass the production of transgenic plants in any number of monocots and edible grains as discussed above. Rye, millet, triticale and sorghum are such a plants, and thus the transformation of these plants is considered to be encompassed by the teachings of van Ooijin et al.

While the examiner believes that adequate motivate to make the claimed invention is provided by the above rejection, Shi *et al.* provide further motivation to make transgenic plants that produce thioredoxin h. Shi *et al.* experiments in which they transformed tobacco plants with thioredoxin h for the purpose of studying thioredoxin h activity in plants (p. 654 and 657). Shi *et al.* further teach that thioredoxins are active in many biochemical processes in plants (p. 654). Shi *et al.* teach eight day old plants and mature plants with pods, and further teach analysis of transgenic seeds (p. 658, Col. 2). Thus, the combined teachings of van Ooijen et al., Bower *et al.* and Shi *et al.* would have further motivated the production of monocot plants expressing transgenic thioredoxin h molecules. The teachings of Bower *et al.* provide a thioredoxin of interest, the teachings of van Ooijen specifically provide methodology for the transformation of monocots, and Shi *et al.* demonstrate that the production of transgenic plants producing thioredoxin h is of interest in elucidating the functionality of thioredoxin h in plants. Thus, it

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would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made transgenic plants expressing these thioredoxin h molecules. The ordinary practitioner would have been motivated to transform transgenic plants with these molecules in order to further study the biological function of the thioredoxin h polypeptides plants, or as an alternative method for producing thioredoxin h polypeptides for study. The ordinary practitioner would have been motivated by the success of Shi *et al.*'s expression of thioredoxin to extend this method to the thioredoxin molecules taught by Bower *et al.* The ordinary practitioner would have also been motivated by the teachings of van Ooijen et al. to produce specifically monocot plants producing thioredoxin h in order to study the activity of this polypeptide in monocot plants.

Thus for all of these reasons, the rejected claims are prima facie obvious in view of the prior art.

- 13. Claims 36-37 and 79-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over (A) van Ooijen et al. in view of Ishiwatari *et al.* (Planta, 1995, 195(3)456-463), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 119, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 139, 140, 142, 144, 146, and 148 above, and further in view of Marris et al. (Plant Molecular Biology 10:359-366 (1988)) OR
- (B) as being unpatentable over van Ooijen et al. in view of Gautier *et al.* (1998, European Journal of Biochemistry, 252:314-324), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 38, 39, 40, 41, 42,

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77, 81, 82, 83, 84, 85, 112, 114, 116, 119, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 139, 140, 142, 144, 146, and 148 above and further in view of Marris et al. (Plant Molecular Biology 10:359-366 (1988)) OR

- (C) as being unpatentable over van Ooijen et al. (US 5543576) in view of Rivera-Madrid et al. (PNAS USA, 92:5620-5624 (1995)), and optionally, both of these further in view of Shi *et al*. (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, and 152 above, and further in view of Marris et al. (Plant Molecular Biology 10:359-366 (1988)) OR
- (D) as being unpatentable over van Ooijen et al. (US 5543576) in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 151, and 153 above, and further in view of Marris et al. (Plant Molecular Biology 10:359-366 (1988)) OR
- (E) as being unpatentable over van Ooijen et al. (US 5543576) in view of Brugidou et al. (Mol. Gen. Genet (1993) 238:285-293), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 154, and 156 above, and further in view of Marris et al. (Plant Molecular Biology 10:359-366 (1988)) OR
- (F) as being unpatentable over van Ooijen et al. (US 5543576) in view of Bower et al. (The Plant Cell, Vol. 8:1641-1650), and optionally, both of these further in view of Shi et al. (Plant

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Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 155 and 157 above, and further in view of Marris et al. (Plant Molecular Biology 10:359-366 (1988)).

The teachings of van Ooijen et al., Ishiwatari et al., Shi et al., Gautier et al., Rivera-Madrid et al., Bower et al., and Brugidou et al. are applied to this rejection as discussed in the previous rejections. None of these previously cited references teach the use of a barley B1 Hordein promoter. However, van Ooijin et al. do specifically teach that "Regulatory sequences which are known or are found to cause sufficiently high expression...of the recombinant DNA in seeds, can be used in the present invention...These include, but are not limited to, promoters from seed-specific genes, especially those of storage protein genes (Col. 7, lines 50-54 and 59-60)." Thus, van Ooijin et al. teach that alternative regulatory sequences can be used with their invention.

Marris et al. teach the barley B₁-hordein regulatory regions localization of expressed proteins in the endosperm, and demonstrate its use to express heterologous proteins in tobacco. Marris et al. teach that "the nucleotide sequences necessary for tissue and developmental expression are present in the 549 bp 5' flanking region of the B1 hordein gene (p. 365)."

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the regulatory sequences taught by Marris *et al.* to produce transgenic plants as taught by the methods taught by any one of (A) van Ooijen et al. in view of Ishiwatari *et al.*, and optionally, both of these further in view of Shi *et al.*, (B) van Ooijen et al. in view of Gautier *et al.*, and optionally, both of these further in view of Shi *et al.*,

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(C) van Ooijen et al. in view of Rivera-Madrid et al., and optionally, both of these further in view of Shi *et al.*, (D) van Ooijen et al. in view of Shi *et al.*, (E) van Ooijen et al. in view of Brugidou et al., and optionally, both of these further in view of Shi *et al.*, or (F) van Ooijen et al. in view of Bower et al. and optionally, both of these further in view of Shi *et al.* The ordinary practitioner would have been motivated by the teachings of Marris *et al.* that the barley B1-hordein promoter drives endosperm specific expression and by the teachings of van Ooijen et al. that other regulatory sequences can be used in to produce transgenic plants according to their invention.

- 14. Claims 36, 37, 43, 79, 80, and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over
- (A) van Ooijen et al. in view of Ishiwatari et al. (Planta, 1995, 195(3)456-463), and optionally, both of these further in view of Shi et al. (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 119, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 139, 140, 142, 144, 146, and 148 above, and further in view of Brandt et al. (Carlsberg Res. Commun. Vol. 50, p. 333-345 (1985)) OR
- (B) as being unpatentable over van Ooijen et al. in view of Gautier *et al.* (1998, European Journal of Biochemistry, 252:314-324), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 119, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 139, 140, 142, 144, 146, and 148 above and further in view of Brandt et al. (Carlsberg Res. Commun. Vol. 50, p. 333-345 (1985)) OR

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(C) as being unpatentable over van Ooijen et al. (US 5543576) in view of Rivera-Madrid et al. (PNAS USA, 92:5620-5624 (1995)), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, and 152 above, and further in view of Brandt et al. (Carlsberg Res. Commun. Vol. 50, p. 333-345 (1985)) OR

- (D) as being unpatentable over van Ooijen et al. (US 5543576) in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 151, and 153 above, and further in view of Brandt et al. (Carlsberg Res. Commun. Vol. 50, p. 333-345 (1985)) OR
- (E) as being unpatentable over van Ooijen et al. (US 5543576) in view of Brugidou et al. (Mol. Gen. Genet (1993) 238:285-293), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 154, and 156 above, and further in view of Brandt et al. (Carlsberg Res. Commun. Vol. 50, p. 333-345 (1985)) OR
- (F) as being unpatentable over van Ooijen et al. (US 5543576) in view of Bower et al. (The Plant Cell, Vol. 8:1641-1650), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140,

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142, 144, 146, 148, 155 and 157 above, and further in view of Brandt et al. (Carlsberg Res. Commun. Vol. 50, p. 333-345 (1985)).

The teachings of van Ooijen et al., Ishiwatari et al., Shi et al., Gautier et al., Rivera-Madrid et al., Bower et al., and Brugidou et al. are applied to this rejection as discussed in the previous rejections. None of these previously cited references teach the use of a barley B1 Hordein promoter or signal sequence. However, van Ooijin et al. do specifically teach that "Regulatory sequences which are known or are found to cause sufficiently high expression...of the recombinant DNA in seeds, can be used in the present invention...These include, but are not limited to, promoters from seed-specific genes, especially those of storage protein genes (Col. 7, lines 50-54 and 59-60)." Thus, van Ooijin et al. teach that alternative regulatory sequences can be used with their invention. In addition, van Ooijin et al. suggest the use of heterologous signal sequences, and teach that especially preferred signal sequences are signal sequences obtained from seed storage proteins (Col. 8, lines 17-19).

Brandt et al. teach the promoter and nucleic acid encoding the signal sequence from a B1 hordein gene from barley, which is a seed storage protein (p. 337-338; Fig. 4).

Thus, it would have been prima facie obvious to one of ordinary skill in the art to have modified the methods taught by any one of (A) van Ooijen et al. in view of Ishiwatari et al., and optionally, both of these further in view of Shi et al., (B) van Ooijen et al. in view of Gautier et al., and optionally, both of these further in view of Shi et al., (C) van Ooijen et al. in view of Rivera-Madrid et al., and optionally, both of these further in view of Shi et al., (D) van Ooijen et al. in view of Shi et al., (E) van Ooijen et al. in view of Brugidou et al., and optionally, both of these further in view of Shi et al., or (F) van Ooijen et al. in view of Bower et al. and optionally,

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both of these further in view of Shi *et al.* by the use of the promoter and signal sequence taught by Brandt et al. The ordinary practitioner would have been motivated to have made such a modification in order to have provided an alternative methodology for the practice of the cited methods, since van Ooijen et al. clearly suggest the use of alternative regulatory sequences and signal sequence, especially from seed storage proteins.

Response to Remarks

Applicants pointed out that the prior art provides a number of thioredoxin molecules, and amended the claims to thioredoxin from plant species for which nucleic acids encoding at least one thioredoxin h have been provided in the specification or in the prior art. The written description rejection has been modified in light of this disclosure.

Applicants amendment to the claims and comments with regard to Rodriguez have been addressed in the new grounds of rejection set forth herein. In particular, van Ooijen et al. teaches the use of maturation specific promoters.

The examiner confirmed via telephone calls and e-mails to a number of libraries (National Library of Medicine, Michigan State University, University of Illinois, Urbana Champaign, and the USPTO STIC) and the publisher of the journal that the Cho et al. reference was not available prior to the priority date of the instant application. Thus, the Cho et al. reference is a 102(a) type reference with regard to its date. The rejection in view of Cho et al. has been withdrawn in light of applicant's declaration which removes the reference as a 102(a) type reference because it is no longer considered to be "by another" (see MPEP 2132.01).

Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C Einsmann

Examiner Art Unit 1634

September 30, 2002

Supervisory Patent Examiner Technology Center 1600